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THE CONTENT OF CATECHOLAMINES IN THE ADRENAL GLANDS
AND SECTIONS OF THE BRAIN UNDER HYPOKINESIA
AND INJECTION OF SOME NEUROTROPIC AGENTS

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16. Abstract White rats (75) were studied. Profound changes in body catecholamine balance occurred as a result of prolonged acute restriction of motor activity. Adrenalin retention increased and noradrenalin retention decreased in the adrenal glands, hypothalamus, cerebral hemispheres, cerebellum and medulla oblongata. Observed alterations in catecholamine retention varied depending upon the type of neurotropic substance utilized. Melliipramine increased catecholamine retention in the tissues under observation, while spasmolytin brought about an increase in adrenalin concentration in the adrenals and a decrease in the brain.					
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THE CONTENT OF CATECHOLAMINES IN THE ADRENAL
GLANDS AND SECTIONS OF THE BRAIN UNDER HYPO-
KINESIA AND INJECTION OF SOME NEUROTROPIC AGENTS

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In experiments on rats it was established that, under the /45*
influence of comparatively prolonged acute restriction of motor
activity, profound alterations in the catecholamine balance occur,
manifested as an increase in the content of epinephrine and decrease
in the content of norepinephrine in the adrenals, hypothalamus,
cerebral hemispheres, cerebellum, and medulla oblongata. It was
shown that the observed alterations in catecholamine content may
be compensated through the use of corresponding neurotropic substances.
Mellipramine facilitates an increase in the content of catecholamines
in the tissues under study, while spasmolytin causes an increase in
the concentration of epinephrine in the adrenals and a decrease in
the brain.

The harmful effects of decreased motor activity (hypokinesia)
on the condition of human and animal body physiological functions
have recently become of increasing interest to biologists and
physicians. It has been established that restriction of motor activity
invariably leads to disorders in a number of metabolic processes
and physiological systems which function as regulators, for example,
those producing hormones and mediators, in particular catecholamines
[2,3,5,7,8].

Catecholamines are present in various functional and struct-
ural regions of the brain and adrenals, and play an important role
in the mechanisms of physiological processes. In this connection,
the search for substances which normalize disordered catecholamine
metabolism in the body and ways of using neurotropic pharmacological

substances is assuming great practical significance.

We studied the dynamics of catecholamine content in the adrenals and in various regions of the brain during acute restriction of body motor activity.

Experiments were conducted on white laboratory rats of both sexes. 75 animals were used, having pre-experiment weights of 160-200 g.

In experiments of the first series, the change in catecholamine content in the organs under study was examined following 7, 14, and 21 days of acute motor activity restriction. In experiments of the second series, the same indices were studied following 7 and 14 days of motor activity restriction, with daily injection of neurotropic substances into the experimental animals. One of the animal groups received injections of mellepramine, 6mg. per 1kg. body weight, and the other received spasmolytin, 4mg /kg over the course of the entire experiment. Intact rats kept under normal vivarium conditions without restricting activity served as the control. /46

In order to create hypokinesia, the animals were placed in special panelled cages, set up according to the shape and size of the animal. The construction of the cages permitted systematic removal of food wastes, urine, and fecal substances, and supplied water and feed to the animals. The animals received unlimited quantities of water and food. The cages and animals were kept at a relatively constant temperature and received moderate natural illumination. Before placing the rats in the cages, they were weighed and their temperatures taken. Over the course of the entire experiment, body weights of the experimental and control rats were taken and rectal temperature was recorded daily. The results of the measurements were worked up using variation statistics and Student's method.

At a preselected time, the rats were decapitated and the content of catecholamines (epinephrine and norepinephrine) in the organs and tissues was determined. Epinephrine and norepinephrine content in

the adrenals and various regions of the brain (hypothalamus, cerebral hemispheres, cerebellum, and medulla oblongata) was determined using V. O. Osinskaya's fluorometric method [6]. Fluorescent intensity was measured using a PF-1 domestic brand fluorometer, using excitation waves of 360 nanometers, obtained from a URS-3 primary light filter. Maximum fluorescence corresponded to a frequency of 510 nanometers, obtained through a secondary interference light filter.

Analysis of the statistical data indicates that hypokinesia over the course of the entire experiment caused a trustworthy progressive increase in epinephrine content in the adrenals (Table 1). Thus, following seven days of hypokinesia, epinephrine content in the adrenals increased almost two times, while following 21 days it increased almost five times relative to the controls.

Change in norepinephrine content in the adrenals occurred in two phases: a decrease took place on the 7th day of the experiment, while on the 14th day there was a maximum increase in the quantity of this substance in the adrenals. The decrease in norepinephrine concentration in the adrenals, apparently, was a consequence of elevated output of it into the blood, and was probably associated with the passive anxiety of the animals.

Acute restriction of motor activity caused considerable fluctuations in the concentration of catecholamines in the brain tissues under study, which undoubtedly is evidence of alteration in the mechanisms of nervous processes. By the 7th day of the experiment, epinephrine content in the hypothalamus increased almost 5 times relative to controls, and in the cerebral hemispheres increased 3 times. A noticeable increase in the quantity of epinephrine was also established in the cerebellum and medulla oblongata following 7 days of acute hypokinesia. Further increase in epinephrine content in both the hypothalamus and cerebral hemispheres occurred by the 14th day of the experiment. In the cerebellum and medulla oblongata,

the quantity of epinephrine did not change, or perhaps decreased somewhat, in comparison to the 7th day of the experiment; by the 21st day, a further moderate increase in epinephrine content was noted in the hypothalamus, cerebellum, and medulla oblongata (Table 1).

Acute restriction of the animals' motor activity caused an increase in the concentration of norepinephrine in all the regions of the brain under study: in the medulla oblongata - over the course of the entire experiment, in the hypothalamus, cerebellum, and cerebral hemispheres - by the 14th and 21st days of the experiment.

The considerable alteration in the distribution of catecholamines in various regions of the brain during hypokinesia must be examined within the framework of autoregulatory neurohumeral processes. The high content of epinephrine and products of its oxidation were evidence of intensification of metabolic processes, which may lead to tissue hypoxia. Moreover, the large quantity of catecholamines changes the energy balance, which is harmful to the overall functional condition of the body. In particular, energy balance disorders manifest themselves in processes associated with acetylcholine synthesis, and may have an effect on the functional condition of the nervous system as a whole.

Results of experiments using injection of neurotropic substances into immobilized animals are of considerable interest (Table 2). In the first stage of the experiment, the neurotropic preparation mellepramine caused a distinct increase in epinephrine and norepinephrine content in the animal tissues under study, in comparison to the tissues of animals which were kept immobilized but did not receive mellepramine. Epinephrine concentration in brain tissues began to gradually decrease on the 14th day.

Norepinephrine content in brain tissues grew sharply in the 1st half of the experiment, and on the 14th day it continued to be

higher than in animals subjected only to immobilization. Upon the injection of mellepramine, norepinephrine content decreased so abruptly that we could not detect it. This fact may be evidence of sympatico-adrenal system function exhaustion, which is an unfavourable symptom and must be taken into account when making an overall evaluation of the reactivity of the body to prolonged hypokinesia. It has been suggested [4] that mellepramine, as an antidepressant, has an effect at least on 2 regions of the brain: the hypothalamus, in its posterolateral regions, and the amygdaloid complex, in its basiolateral part.

Injection of the immobilized animals with spasmolytin caused a two phased change in epinephrine content in the adrenals: a considerable increase was noted following 7 days, and a sharp decrease of epinephrine content in the adrenals relative to controls (immobilized animals) was noted following 14 days.

Injection of spasmolytin and immobilization over the entire course of the experiment caused a moderate decrease in epinephrine content in the brain tissues under study. Following injection of spasmolytin, norepinephrine quantity in the adrenals of the immobilized rats decreased sharply following seven days and continued to decrease for 14 days of the experiment. Norepinephrine content increased in the brain tissues, with the exception of the cerebellum. /49

The effect of spasmolytin on the indices we studied may be explained by blocking of the cholinergic system of the cerebral cortex and hippocampus, since we know that expanded cortical inhibition causes an increase in the content of norepinephrine in brain tissue[1].

The results of the second series of experiments indicated that alterations in catecholamine content observed in various tissues during immobilization may be successfully modified through injection of the corresponding neurotropic substances.

All of the above leads us to conclude that protracted hypokinesia causes profound changes in catecholamine metabolism in animals, which is manifested by an increase in epinephrine content and decrease in norepinephrine quantity in all tissues under study. The nervous system stimulator mellepramine causes an increase in catecholamine content for the tissues under study in such animals. The N-cholinolytic spasmolytin increases epinephrine content in the adrenals during hypokinesia, and decreases its quantity in brain tissues.

TABLE 1. CHANGE IN CATECHOLAMINE CONTENT IN THE ORGANS OF RATS FOLLOWING ACUTE RESTRICTION OF MOTOR ACTIVITY

Cond'ns of Exprmnt	Number of Animals	Catecholamine content, micrograms per lg. raw tissue									
		adrenals		hypothalamus		cerebral hemispheres		cerebellum		medulla oblongata	
		A	N	A	N	A	N	A	N	A	N
Control..	6	1316±75	333±34.3	1.9±0.32	3.73±0.34	0.389±0.126	0.512±0.142	0.525±0.095	1.04±0.012	0.888±0.282	0.51±0.093
7 days Immobil'n	9	2315±98 P<0.001	282±30.77 P<0.1	6.24±0.90 P<0.001	2.0±0.75 P<0.05	3.24±0.67 P<0.001	0.49±0.079 P<0.1	2.2±0.35 P<0.001	0.55±0.095 P<0.001	1.28±0.27 P<0.1	0.92±0.19 P<0.05
14 days Immobil'n	8	3163±198 P<0.001	465±36.5 P<0.02	7.27±0.58 P<0.001	1.62±0.37 P<0.001	4.39±0.94 P<0.001	0.844±0.1 P<0.1	2.17±0.27 P<0.001	1.21±0.15 P<0.1	1.08±0.2 P<0.1	1.40±0.20 P<0.02
21 days Immobil'n	9	5220±416 P<0.001	351±29.27 P<0.1	10.73±0.95 P<0.001	5.48±0.54 P<0.01	1.81±0.3 P<0.001	1.91±0.28 P<0.001	2.22±0.31 P<0.001	1.78±0.19 P<0.002	1.53±0.26 P<0.1	1.61±0.41 P<0.02

Key: A -- adrenaline
N -- noradrenaline

TABLE 2. CATECHOLAMINE CONTENT IN THE ORGANS OF RATS FOLLOWING ACUTE RESTRICTION OF MOTOR ACTIVITY AND INJECTION OF NEUROTROPIC SUBSTANCES

Cond'ns of Exprmnt	Number of Animals	Catecholamine content, micrograms per lg. raw tissue									
		adrenals		hypothalamus		cerebral hemispheres		cerebellum		medulla oblongata	
		A	N	A	N	A	N	A	N	A	N
7 days Immobil'n	5	2274±95.57	270±22.8	5.5±0.508	2.45±0.562	2.48±0.481	0.45±0.077	2.8±0.106	0.5±0.111	1.13±0.185	0.89±0.13
14 days Immobil'n	6	2992±150.6	470±35.5	6.93±0.542	1.75±0.2	4.02±0.71	0.871±0.012	2.07±0.278	1.28±0.15	1.12±0.153	1.31±0.111
7 days Imm. +melliprnm	8	3206±385 P<0.05	0	11.25±2.6 P<0.05	20.0±2.88 P<0.01	4.24±0.45 P<0.1	2.33±0.45 P<0.05	3.5±0.62 P<0.1	2.33±0.54 P<0.05	2.77±0.57 P<0.02	4.42±0.6 P<0.002
14 days Immobil'n +melliprnm	8	2723±424.4 P<0.1	0	1.66±0.41 P<0.001	12.08±2.31 P<0.05	1.25±0.38 P<0.02	2.1±0.86 P<0.1	1.41±0.54 P<0.002	1.70±0.63 P<0.1	1.27±0.14 P<0.1	2.08±6.24 P<0.05
7 days Immobil'n +spasmoltn	8	7370±592 P<0.001	0	2.08±0.41 P<0.002	4.58±0.41 P<0.01	2.2±0.93 P<0.1	1.86±0.19 P<0.001	1.33±0.77 P<0.1	0	1.05±0.46 P<0.1	3.86±1.37 P<0.02
14 days Immobil'n +spasmoltn	8	136±12.0 P<0.001	220±90.7 P<0.1	3.3±0.42 P<0.01	5.83±0.41 P<0.1	1.16±0.3 P<0.01	1.5±0.29 P<0.001	1.25±0.29 P<0.05	7.16±0.91 P<0.001	0.6±0.005 P<0.02	3.99±1.06 P<0.05

Key: A -- adrenaline
B -- noradrenaline

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